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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,577	12/16/2005	Tetsuro Kikuchi	Q86357	6428

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EXAMINER	
GRAHAM, SHELLEY R	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
03/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,577	KIKUCHI ET AL.	
	Examiner	Art Unit	
	SHELLEY R. GRAHAM	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *9-12,21-24 and 33-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,13-20 and 25-32* is/are rejected.

7)☒ Claim(s) *9-12,21-24 and 33-36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :1 sheet (15 Nov 2007), 1 page (21 Feb 2006), 5 pages (15 July 2005), 1 page (03 November 2006).

DETAILED ACTION

Status of the Application

Claims 1-19 are being examined on their merits.

Objections

Claim Objection

1. Claims 9-12, 21-24 and 33-36 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, claims 9-12, 21-24 and 33-36 have not been further treated on the merits.

Rejections

Use Claims

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13-20 provides for the use of a pharmaceutical composition comprising at least one carbostyril derivative in combination with at least one serotonin reuptake inhibitor; however, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending the claims to teach. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

3. Claims 13-20 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example Ex parte Dunki, 153 USPQ 678 (Bd.App. 1967) and Clinical Products, Ltd. v. Brenner, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

4. Claims 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what applicant intends by the word "use" as to whether the claims are product or process claims.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Lack of Antecedent Basis Rejection - 35 USC § 112 2nd

5. Claims 5-7, 17-19, and 29-31 are rejected under U.S.C. 112, second paragraph. Claims 5, 17, and 29, which are dependent from claims 4, 16, and 28, respectively, recite "the metabolite of

aripiprazole is…DCPP". However, DCPP is not a carbostyril derivative as is required in claims 4, 16, and 28. Therefore claims 5, 17, and 29 lack antecedence in claims 4, 16, and 28, respectively. Claims 6-7, 18-19, and 30-31 depend from claim 5, 17, and 29, respectively, and therefore the issues with claims 5, 17, and 29 are also contained in claims 6-7, 18-19, and 30-31 due to their dependence from claims rejected claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Lack Scope of Enablement Rejections - 35 USC § 112 1st

6. Claims 13-20 and 25-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating depression and major depressive disorder, does not reasonably provide enablement for treating other disorders known to man. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

7. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

8. The present invention of claims 13-20 is drawn to a pharmaceutical composition comprising at least one carbostyril derivative in combination with at least one serotonin reuptake inhibitor, in the preparation of a medicament for treating disorders. While claims 25-32 are drawn to a method of treating disorders in a patient comprising administration of an effective amount of a pharmaceutical composition comprising at least one carbostyril derivative in combination with at least one serotonin reuptake inhibitor.

The breadth of the claims

9. Claims 13-20 and 25-32 encompass a pharmaceutical composition for treating disorders. It is noted that any disease may represent a "disorder". Therefor Applicants are claiming that the composition can treat any and all disorders known to man.

Quantity of Experimentation

10. The quantity of experimentation in this area is large since there is no reasonable expectation of success as the methods are not fully outlined in the specification. The specification only discloses working examples of treatments for depression and major depressive disorder. It is unclear in the specification how the plurality of diseases claimed can be treated by the claimed invention. The specification fails to address this issue.

Working Examples

11. The specification has several examples, however, aripiprazole is the only tested compound and the tests and assays conducted are indicative for treatment of depression only.

The unpredictability of the art and the state of the prior art

12. It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). The relative skill of the artisan or the unpredictability of the pharmaceutical art is very high. Where the physiological activity of a chemical or biological compound is considered to be an unpredictable art (Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved" (See In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)), the skilled artisan would have not known how to extrapolate the results provided in the instant specification to the larger and varied genus of treatment of all disorders that currently exist or may exist in the future.

Guidance in the Specification

13. The examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient guidance or direction as to how to make and use the full scope of the instant claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of any carbostyril

derivative in combination with any serotonin reuptake inhibitor for the full scope of the presently claimed subject matter. In the absence of such guidance and evidence or reasoning, the specification fails to provide an enabling disclosure.

Level of Skill in the Art

14. The level of skill in the art is deemed to be high.

Conclusion

15. In the instant case, as discussed above, the specification provides one with no written description or guidance that leads one to a readily ascertain which disorders are treatable by any one carbostyril derivative in combination with any one serotonin reuptake inhibitor. Thus given the an art whose nature is identified as unpredictable, the lack of guidance in the specification, the large quantity of research required to determine the correct methodology to employ, the presence of limited examples utilizing a working protocol, it is concluded that it would require undue experimentation for one of skill in the art to perform the method of the claims as written.

Lack of Written Description Rejections - 35 USC § 112 1st

16. Claims 1-8, 13-20 and 25-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. The "carbostyril derivative" and "Metabolite of aripiprazole" limitations lack written description of what chemicals or chemical structures that applicant had possession of. A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variations with in the genus. See MPEP 2163.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3, 6, 8, 13-15, 18, 20, 25-27, 30 and 32 are rejected under 35 U.S.C. 102(b), as being anticipated by WONG et al. (US 2002/0156067 A1, 24 October 2002).

19. WONG et al. teach compositions comprising a) one or more norepinephrine reuptake inhibitors and b) one or more neuroleptic agents (WONG claim 1). Among the compounds listed for component a) are duloxetine, venlafaxine, and milnacipran (WONG claim 2). These are the identical compounds listed as examples of serotonin reuptake inhibitors useful in the instant application (instant app claims 6, 18 and 30). Among the compounds listed by WONG et al. as neuroleptic agents, component b), is aripiprazole (WONG claim 5). This is the exact compound presented in the instant application as a carbostyril derivative (instant app claims 3, 15 and 27).

20. Example 2 (WONG et al.) describes the preparation of the composition, in that the active components are combined in a pharmaceutically acceptable carrier (WONG page 6, column 1, paragraph 47, lines 1–3). Thus anticipating instant application claims 8, 20 and 32.

21. Claims 1, 2, 5, 9 and 19 (WONG et al.) describes the composition, the use of the composition of their invention for treating diseases or disorders of the central nervous system, and a method for treating a disease or disorder of the central nervous system comprising administering the composition of their invention, anticipating instant claims 1, 13 and 25.

22. It is respectfully pointed out that instant claims 2, 14 and 26 describe a property of the carbostyril derivative as being a dopamine-serotonin system stabilizer, wherein the carbostyril derivative is aripiprazole according to claim 3. If indeed aripiprazole is a dopamine-serotonin system stabilizer in the instant application, the same would hold true about aripiprazole as a dopamine-serotonin system stabilizer in WONG et al. This being so, as the aripiprazole in the instant application and aripiprazole in WONG et al. is the same compound.

23. Thus WONG et al. anticipate each and every aspect of the rejected claims 1-3, 6, 8, 13-15, 18, 20, 25-27, 30 and 32 of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shelley R. Graham, whose telephone number is 571-270-1563. The examiner can normally be reached on M-R 8am-3pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRG
04 February 2008

/Zohreh A Fay/
Primary Examiner, Art Unit 1612